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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/070,633	03/04/2002	Joanne Elizabeth Anderson	PU3703USW	9460

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EXAMINER
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SHIBUYA, MARK LANCE

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 07/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/070,633

Applicant(s)

ANDERSON ET AL.

Examiner

Mark L. Shibuya

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 March 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-8, 11 and 13 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8, 11 and 13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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### DETAILED ACTION

1. Claims 1-8, 11 and 13 are pending and examined.

#### *Withdrawn Claim Rejections*

2. The rejection of Claims 1-5, 9-11, and 13 under 35 U.S.C. 102(b) as being anticipated by Yan et al., J. Org. Chem. (Oct. 18, 1996) Vol. 61, pp. 7467-7472, is withdrawn in view of applicant's amendments to the claims, entered 3/30/2005, requiring a plurality of discrete solid support adhere to the attenuated total reflection element.
3. The rejection of Claims 1-5, 9-11, 13 under 35 U.S.C. 102(a) as being anticipated by Huber et al., Analytica Chimica Acta, vol. 393, (28 July 1999), pp. 213-221, is withdrawn in view of applicant's amendments to the claims, entered 3/30/2005, requiring a plurality of discrete solid support adhere to the attenuated total reflection element.
4. The rejection of Claims 1 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of **Yan et al.**, J. Org. Chem. (Oct. 18, 1996) Vol. 61, pp. 7467-7472; or **Huber et al.**, Analytica Chimica Acta, vol. 393, (28 July 1999), pp. 213-221, each taken separately, as above, and in view of **Zuellig et al.**, (US 6,126,904), is withdrawn in view of applicant's amendments to the claims, entered 3/30/2005,

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requiring a plurality of discrete solid support adhere to the attenuated total reflection element.

***Priority***

5. The instant application is a 371 of PCT/US00/28218, filed 10/12/2000, which claims benefit of 60/159,673, filed 1/15/1999.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-8, 11 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant's amendment necessitated the instant new ground(s) of rejection.

Claim 1, (and its dependent claims), states a typing error in line 7, which is "element ;".

***Maintained Claim Rejections - 35 USC § 102***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

7. Claims 1-5, 11, and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Yan et al., J. Comb. Chem. (1999) Vol. 1, pp. 46-54, (published on Web 12/01/1998).

This rejection maintains the reasons of record as set forth in the previous Office action (repeated below for the convenience of the reader).

Yan et al., throughout the publication and especially at the abstract, p. 47, para 7, p. 48, para 7-p. 49, para 1, Scheme 1 and Figure 1, teach a Attenuated Total Reflection (Macro-ATR) method measuring infrared transmission to monitor solid-phase organic reactions (see Scheme 1) on polystyrene or polystyrene-poly(ethylene glycol) based resin beads.

The claims, as currently amended, are drawn to a method for monitoring a solid phase chemical reaction, said method comprising the steps of: providing a reaction mixture comprising discrete-solid supports and a liquid reaction medium, contacting an attenuated total reaction element to said reaction mixture, a plurality of said discrete solid samples adhering to-said attenuated total reflection element; and then in real time, directly monitoring said chemical reaction on said plurality of discrete solid supports through said attenuated total reflection element, wherein said monitoring step is carried out by attenuated total reflection spectroscopy; and variations thereof.

#### Response to Arguments

Applicant argues that the reference of Yan does not teach direct monitoring as claimed in the present invention. Applicant argues that the instant Yan reference requires removing samples of the reaction suspension (p. 53, col. 3). The Yan reference requires intervening processing steps in order to monitor the reaction.

Applicant's arguments filed 3/30/2005 have been fully considered but they are not persuasive.

Yan, (1999), at p. 47, para 7 and pp. 53-54, bridging paragraph, teach the macro-ATR measurement on approximately 0.2 mg of beads, in distinction to previous single bead, micro-ATR measurements (citing to Yan et al., J. Org. Chem. (Oct. 18, 1996) Vol.

61, pp. 7467-7472, of record). Yan (1999) at pp. 48-49, bridging paragraph, and Figure 1, teaches monitoring ATR spectra.

The examiner respectfully submits that Yan (1999) teaches a direct monitoring of a chemical reaction, in real time, using attenuated total reflection (ATR). The specification must clearly set forth the definition explicitly and with reasonable clarity, deliberateness, and precision. *Teleflex, Inc. v. Ficosa North America Corp.*, 63 USPQ2d 1374, 1381 (Fed. Cir. 2002); *Rexnord Corp. v. Laitram Corp.*, 60 USPQ2d 1851, 1854 (CAFC 2001); and MPEP 211.01. Exemplification is not an explicit definition. Even "explicit definitions" can be subject to varying interpretations. The specification as filed, does not provide a limiting definition of "direct monitoring", such that the teachings of Yan (1999) are overcome.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., that samples not be removed or that no intervening steps occur in order to monitor the reaction) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Nevertheless, Yan (1999) teaches monitoring a chemical reaction directly on beads in contact with a total reflection element (pp. 53-54, bridging paragraph), and without removing samples or intervening steps.

8. Claims 1-4 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Cheng et al., Langmuir (1998) Vol. 14, pp. 839-844, (published on Web 01/23/1998).

This rejection maintains the reasons of record as set forth in the previous Office action (repeated below for the convenience of the reader).

Cheng et al., throughout the publication, and especially at the abstract, p. 840, para 2-7, Figure 1, p. 841, para 3, figure 3, p. 843, para 3, teach attenuated total reflection Fourier transform infrared (ATR-FTIR) to monitor the tethering of phospholipid bilayers to gold-coated, ZnSe crystals (which reads on a solid support bound to the attenuated total reflection element, as in claim 12).

### Response to Arguments

Applicant argues that Cheng does not teach or disclose direct monitoring of the reaction as the reaction occurs on multiple supports adhering to the ATR element.

Applicant's arguments filed 3/30/2005 have been fully considered but they are not persuasive.

Cheng, (1999), at, for example, p. 841, para 2, p. 843, para 3, teaches vesicles, which read on multiple supports, that directly adhere to the ATR element.

The examiner respectfully submits that the specification as filed, does not provide a limiting definition of direct monitoring, such that the teachings of Cheng are overcome. The specification must clearly set forth the definition explicitly and with reasonable clarity, deliberateness, and precision. *Teleflex, Inc. v. Ficosa North America Corp.*, 63 USPQ2d 1374,1381 (Fed. Cir. 2002); *Rexnord Corp. v. Laitram Corp.*, 60 USPQ2d 1851, 1854 (CAFC 2001); and MPEP 211.01. Exemplification is not an explicit definition. Even "explicit definitions" can be subject to varying interpretations. Thus, absent evidence to the contrary, Cheng teaches a "direct monitoring" of multiple supports, using attenuated total reflection (ATR).

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., that samples not be removed or that no intervening steps occur in order to monitor the reaction) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Nevertheless, Cheng teaches monitoring a chemical reaction directly on vesicles in contact with a total reflection element, and without removing samples or intervening steps.

9. Claims 1, 2, 11 and 13 are rejected under 35 U.S.C. 102(e) as being anticipated by Eipel et al., (US 6,737,024). This rejection maintains the reasons of record as set forth in the previous Office action (repeated below for the convenience of the reader).

Eipel et al., (US 6,737,024), effective date Jan. 14, 1999, at col. 1, lines 47-56, col. 2, lines 28-67, Fig. 2, col. 3, lines 46-55 and 65, col. 4, lines 1-16, 37-59, col. 5, lines 5-10 and 31-37, teach methods of combinatorial chemistry using automated solid-phase synthesis, including separate discrete solid supports, where the support may be glass, quartz, silicon, germanium, or polystyrene, and wherein attenuated total reflection is used to measure light absorption. This rejection maintains the reasons of record as set forth in the previous Office action.

#### Response to Arguments

Applicant argues that Eipel does not disclose non-intervening monitoring as claimed.

Applicant's arguments filed 3/30/2005 have been fully considered but they are not persuasive.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies



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(i.e., that no intervening steps occur in order to monitor the reaction) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Nevertheless, Eipel, at col. 4, line 59-col. 5, line 4, teaches monitoring a chemical reaction directly on sites on support surfaces that are, absent evidence to the contrary, in contact with a total reflection element, and without removing samples or intervening steps.

### ***Maintained Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

10. Claims 1 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of **Yan et al.**, J. Comb. Chem. (1999) Vol. 1, pp. 46-54, (published on Web 12/01/1998); **Cheng et al.**, Langmuir (1998) Vol. 14, pp. 839-844, (published on Web 01/23/1998); or **Eipel et al.**, (US 6,737,024), each taken separately, and in view of **Zuellig et al.**, (US 6,126,904). This rejection maintains the reasons of record as set forth in the previous Office action (repeated below for the convenience of the reader).

**Yan et al.**, J. Comb. Chem. (1999) Vol. 1, pp. 46-54, (published on Web 12/01/1998) throughout the publication and especially at the abstract, p. 47, para 7, p. 48, para 7-p. 49, para 1, Scheme 1 and Figure 1, teach a Attenuated Total Reflection (Macro-ATR) method measuring infrared transmission to monitor solid-phase organic reactions (see Scheme 1) on polystyrene or polystyrene-poly(ethylene glycol) based resin beads.

**Cheng et al.**, throughout the publication, and especially at the abstract, p. 840, para 2-7, Figure 1, p. 841, para 3, figure 3, p. 843, para 3, teach attenuated total reflection Fourier transform infrared (ATR-FTIR) to monitor the tethering of phospholipid bilayers to gold-coated, ZnSe crystals (which reads on a solid support bound to the attenuated total reflection element, as in claim 12).

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Eipel et al., (US 6,737,024), effective date Jan. 14, 1999, at col. 1, lines 47-56, col. 2, lines 28-67, Fig. 2, col. 3, lines 46-55 and 65, col. 4, lines 1-16, 37-59, col. 5, lines 5-10 and 31-37, teach methods of combinatorial chemistry using automated solid-phase synthesis, including separate discrete solid supports, where the support may be glass, quartz, silicon, germanium, or polystyrene, wherein the automated systems include metering devices for dispensing liquid, and wherein attenuated total reflection is used to measure light absorption.

None of Yan et al., J. Comb. Chem. (1999) Vol. 1, pp. 46-54, (published on Web 12/01/1998); Cheng et al.; or Eipel et al., (US 6,737,024), teach methods for monitoring a solid phase chemical reaction by attenuated total reflection spectroscopy, wherein the reaction is a Mitsunobu reaction, a Freidel-Craft reaction or a Suzuki reaction.

Zuellig et al., (US 6,126,904), effective filing date of March 7, 1997, at col. 4 line 54-col. 6, line 26, teach synthesis of combinatorial chemical libraries, particularly by employment of solid phase chemistry (col. 5, lines 16-32) and teach that the Suzuki coupling, Mitsunobu reaction, and Friedel-Crafts reaction (as in claims 6-8) are synthetic reactions which may be conducted in solution or on solid phase supports, and are useful in the synthesis of combinatorial chemical libraries.

It would have been *prima facie* obvious at the time the invention was made, for one of ordinary skill in the art to use methods for monitoring a solid phase chemical reaction by attenuated total reflection spectroscopy, wherein the reaction is a Mitsunobu reaction, a Freidel-Craft reaction or a Suzuki reaction.

One of ordinary skill in the art would be motivated to monitor a Mitsunobu reaction, a Freidel-Craft reaction or Suzuki reaction by attenuated total reflection spectroscopy because Eipel et al. teach monitoring of combinatorial chemistry on solid supports using attenuated total reflection and Zuellig et al., teach Suzuki coupling, Mitsunobu reaction, and Friedel-Crafts reaction (as in claims 6-8) are synthetic reactions, which may be conducted in solution or on solid phase supports, and are useful in the synthesis of combinatorial chemical libraries.

The claims, as currently amended, are drawn to a method for monitoring a solid phase chemical reaction, said method comprising the steps of: providing a reaction mixture comprising discrete-solid supports and a liquid reaction medium, contacting an attenuated total reaction element to said reaction mixture, a plurality of said discrete solid samples adhering to-said attenuated total reflection element; and then in real time, directly monitoring said chemical reaction on said plurality of discrete solid supports through said attenuated total reflection element, wherein said monitoring step is carried out by attenuated total reflection spectroscopy; and wherein the reaction is a Mitsunobu reaction, a Freidel-Craft reaction or Suzuki reaction.

### Response to Arguments

Applicant argues that none of the references under 35 USC 102 disclose each and every limitation of the claimed invention and in particular do not disclose the step of directly monitoring the reactions as claimed, and do not disclose the step of contacting an ATR element to the reaction mixture where some of the solid supports then adhere to said ATR element. Applicant argues that the reference of Zuellig et al. does not disclose or suggest the claimed method of contacting the ATR element with the reaction mixture and directly measuring the reaction as claimed.

Applicant's arguments filed 3/30/2005 have been fully considered but they are not persuasive. As stated above, in the response to arguments for the 35 USC 102, the references of Yan et al. (1999), Cheng et al., and Eipel et al. teach the claim limitations. The reference of Zuellig teaches Mitsunobu, Freidel-Craft and Suzuki reactions. For the reasons of record, it would have been obvious at the time the invention was made, for one of ordinary skill in the art to have combined each of Yan et al. (1999), Cheng et al., and Eipel et al., taken separately, with the reference of Zuellig et al. Therefore, a prima facie case of obviousness exists is presented and maintained over the each of the aforementioned references of Yan et al. (1999), Cheng et al., Eipel et al., taken separately, and with the reference of Zuellig et al.

### ***Conclusion***

11. Claims 1-8, 11 and 13 are rejected.

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12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Shibuya whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark L. Shibuya  
Examiner  
Art Unit 1639

  
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PRIMARY EXAMINER

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